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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,033	11/25/2003	Satoru Miyano	34569-701.201	6506
21971 7590 03/22/2007 WILSON SONSINI GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050			EXAMINER WHALEY, PABLO S	
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			1631	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/722,033

Applicant(s)

SATORU MIYANO

Examiner

Pablo Whaley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 18-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/14/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

CLAIMS UNDER EXAMINATION

Applicants' response, filed 12/26/2006, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied, as necessitated by amendment. They constitute the complete set presently being applied to the instant application.

Claims herein under examination are 1-17. Claims 18-26 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant's election was made without traverse on 7/31/06.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement filed 02/14/2007 has been considered in full.

INFORMALITIES

The amendment to the disclosure is acceptable, as the embedded hyperlink has been deleted.

NEW MATTER

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 has been amended to recite a step directed to (d1) mapping a network relationship. In the response filed 12/26/2006, applicant does not point to support for the newly recited limitation. The Examiner has not found support for this limitation in the specification, and this limitation is not present within the scope of the original claims as filed. As the newly recited limitation is not supported by the originally filed claims or disclosure, the claims are rejected for reciting new matter. This rejection is necessitated by amendment.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Applicant's arguments, filed 12/26/2006, and assertion that the claimed method is statutory as it has at least one practical application (i.e. useful result) within the technological arts "as apparent from reading applicant's Specification" is not persuasive for the following reasons.

It is noted that the "practical application in the technological arts" test is no longer the standard. For an updated discussion of statutory considerations, see the Guidelines for Patent

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Eligible Subject Matter in the MPEP 2106, Section IV (Latest Revision August 2006). The revised guidelines specifically state that "a claimed invention is directed to a practical application of a 35 U.S.C. 101 judicial exception when it: (A) "transforms" an article or physical object to a different state or thing; or (B) otherwise produces a useful, concrete and tangible result." As set forth in the previous office action, where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a concrete, tangible, and useful result (i.e. a practical application). The Examiner maintains that claim 1, which is currently amended and now results in "mapping" a network relationship, does not recite a tangible result, as the step directed to "mapping" can reasonably occur within a computer system. Therefore this rejection is maintained and reiterated.

Claims 1-17 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 1-16 are directed to a method for inferring a network relationship between genes, which does not recite either a physical transformation of matter nor a practical application [i.e. concrete, tangible, and useful result]. Therefore, the instant claims encompass non-physical (i.e. *in-silico*) method steps which do not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). In the instant case, claims 1-16 do not recite a tangible result such that it is useful to one skilled in the art. For these reasons, the instant claims are not statutory. This rejection could be overcome by amending the claims to recite that a result of the method is "displayed" or "outputted" (e.g. output to a user, a display, a memory, or another computer, etc.), or by amending the claims to include a step of a physical transformation of matter (e.g. assay). Claim 17 is directed to a

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medium containing one or more results of network relationships between genes calculated using the method of claim 1. The "one or more results" of network relationships recited in the claim is non-functional descriptive material. Non-functional descriptive material stored on a medium is not statutory subject matter (e.g. music stored on a compact disk). In the event that applicant intended for said medium to be "computer-readable medium", it is further noted that computer-readable medium encompasses non-physical media, which is not necessarily directed to a physical product, and therefore is also nonstatutory. For these reasons, the instant claims are not statutory.

LACK OF UTILITY

Applicant's arguments, filed 12/26/2006, do not appear to have addressed the instant utility rejection, per se. However, as applicant's have previously asserted the claimed method has at least one practical application within the technological arts "as apparent from reading applicant's Specification" [Remarks, p.10], the Examiner has taken this to be the applicant's response. Applicant's arguments, however, are not persuasive as they are directed to asserted utilities [0046] and [0047] that are not specific to the instant claims. This rejection is therefore maintained and reiterated.

Claims 1-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well-established utility.

In the instant case, the claimed invention is not supported by a well-established utility. The instant claims generally recite a method for inferring a network relationship between genes. The specification discloses several general disciplines where the development of a gene

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regulatory network from gene expression data may be “useful” in predicting potential therapeutic targets [p.1] and drug development [p. 2]. Furthermore, the specification discloses several methods for inferring gene networks (i.e. interrelations) from expression data such as clustering algorithms, Bayesian networks, and data modeling using a system of differential equations [p.3, ¶ 3 and p. 4, ¶ 1]. It is noted that instant claim 1 recites “generating a set of linear differential equations” and solving equations to produce said network. However, as instant claim 1 is directed to a method for “inferring a network relationship” this utility is not specific to the instant claims. For these reasons, the claimed subject matter does not have a specific, substantial, and credible utility.

Claims 1-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments, filed 07/13/2006, that the instant enablement rejection is improper in view of the detailed description and the examples in the Specification. However, applicant did not distinctly and specifically point to any particular sections of the Specification to support this

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assertion, nor did applicant address any of the Examiner's contentions as set forth in the previous office action, nor did the applicant specifically point out how the amendments to the instant claims would serve to overcome this rejection. Therefore this rejection is maintained and reiterated.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below which leads to the determination that the above claim lacks enablement due to undue experimentation being required to make and use the invention.

In the instant case, the claimed subject matter lacks enablement for the following reasons: Claim 1 is directed to a method for inferring a network relationship between genes requiring (i) providing a quantitative time course data library for a set of genes, (ii) creating a sparse matrix

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having zero coefficients removed therefrom, (iii) generating a set of linear differential equations, and (iv) solving said set of equations to produce said network relationship.

Given the nature of the invention, inferring a network relationship between genes requires inference algorithms to develop an inference model from experimental data such that one skilled in the art would be able to “infer” a network relationship between genes [See 112 2nd rejection below]. However, there are no such limitations recited in the instant claims [Wands factors (2), (4), (8)]. It is noted that instant claim 1, steps (b)-(d) do not necessarily imply the creation of a model and/or modeling of genetic data for inferring a network relationship between genes.

Methods for inferring qualitative relationships in genetic networks from time series data of gene expression patterns are well known in the art [Akutsu et al., Bioinformatics, 2000, Vol. 16, No 8, p.727-734]. Furthermore, methods modeling gene expression data using differential equations and temporal gene expression data are also well known in the art [Chen, Pacific Symposium on Biocomputing, 1999, p.29-40]. Such methods teach the development of inference algorithms, the use of differential equations, techniques for parameter determination (e.g. using linear regression), model specific variables (e.g. mRNA concentrations, protein concentrations, etc.), and the development of qualitative network models for inferring qualitative relationships in genetic networks. It is noted that the instant claims and specification disclose a “sparse matrix” and linear differential equations. However, the specification fails to disclose or provide working examples as to how one skilled in the art would know which parameters and/or variables to use in the construction of the said “sparse matrix” from a quantitative time course library, as in instant claim 1, step (b). Furthermore, the specification fails to disclose or provide working examples as to how one skilled in the art would be able to infer a network relationship between genes using the said “sparse” matrix and the related linear differential equations as recited in instant claim 1, steps (c) and (d) [Wands factors (2), (3)].

Given the nature of the instantly claimed invention, an inference or network model would need to be developed for modeling gene expression and thereby inferring a network relationship between genes. Sufficient information and guidance is required to develop, test, and validate such an inference model, as supported by the teaching of the prior art, above. Prior art [Akutsu et al., p.733, Col. 1, ¶ 1] also teaches that the application of inference methods to real data are difficult for reasons such as noise, modeling assumptions (e.g. time delays, mRNA concentration data), and biological complexity. Although the level of skill in the art of inferring network relationships from time series gene expression data and modeling gene expression with differential equations is high, as insufficient guidance has been given with regards the development of an inference model for inferring a network relationship, as discussed in detail above, one skilled in the art would require undue experimentation to predictably practice the instantly claimed invention [Wands factors (1), (2), (6), (7)].

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These rejections are maintained or necessitated by amendment.

Amended claim 1, step (d1), now recites the limitation "mapping said network relationship." As mapping is inherently a process that occurs between at least two elements (e.g. one-to-one mapping), it is unclear what said mapping is occurring between (i.e. genes, time points, etc.). Clarification is requested. This rejection is necessitated by amendment.

Claim 1, step (b), recites the limitation "creating a sparse matrix." Applicant's arguments did not point to specific points in the Specification wherein "sparse" is exemplified that would serve to clarify the issue, therefore this rejection is maintained and reiterated. As the specification does not define or fully and completely describe "sparse" for carrying out the intended function, it is unclear as to the metes and bounds intended by applicant for the claimed "sparse matrix" such that one skilled in the art would know which steps creating a "sparse" matrix consists of. Clarification is again requested.

Claim 1, step (b), recites the limitation "said matrix having zero coefficients removed therefrom." Applicant's arguments point out that one of skill in the art "would have difficulty in appreciating the removing zero coefficients is part of creating sparse matrix." As applicant's arguments did not clarify the issue, this rejection is maintained and reiterated. It is unclear whether said removal step is intended to be an actual method step or a further limitation of the said "matrix." If applicant intends for the removal of zero coefficients to be part of the claimed method, the claim should be amended to specifically recite this limitation using active language. Clarification is again requested.

Claim 17 recites a "medium containing one or more results of network relationships between genes calculated using the method of claim 1." The Examiner maintains that the term "medium" involves a level of ambiguity in light of the specification. This rejection is maintained and reiterated. As the specification does not define or fully and completely describe "medium" for carrying out the intended function, and as the specification also disclose an "MMGE medium"

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[p.12 and 15], it is unclear as to the metes and bounds intended by applicant for the claimed "medium." Clarification is again requested. Claims 2-16 are rejected as they depend directly or indirectly from rejected claim 1.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant's arguments, filed 12/26/2006, that (i) Chen does not suggest creating a sparse matrix, with the matrix having zero coefficients removed therefrom, and (ii) the Office Action acknowledges this asserted deficiency of Chen are not persuasive for the following reasons.

Regarding (i): Chen clearly teaches transcription matrices representing gene regulatory networks, wherein said matrices comprise "non-zero" elements [p.35, Minimum Weight Solutions to Linear Equations]. As the instant claims do not require as step directed to "removing zero coefficients", the Examiner has broadly and reasonably interpreted Chen as an implicit teaching for "sparse" matrices. Furthermore, Chen teaches methods for developing Boolean networks describing relationships between genes based on time course of expression

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[p.30, ¶ 2 and 4], which the Examiner has broadly interpreted as mapping a network relationship, as in amended claim 1.

Regarding (ii): The previous office action does not acknowledge applicant's assertion that Chen does not suggest creating a sparse matrix, with the matrix having zero coefficients removed therefrom. However, the Examiner did not that because the claims recite the limitation "sparse matrix" which is indefinite (see 112, 2nd), this limitation was interpreted broadly for purposes of applying prior art. For the above reasons, the Examiner maintains that Chen teaches all of the required limitations for claims 1 and 3. Therefore this rejection is maintained and reiterated.

Claims 1 and 3 are rejected under 35 U.S.C. 102 (b) as being anticipated by Chen [Pacific Symposium on Biocomputing, 1999, p.29-40].

Chen teaches methods for modeling gene expression data using differential equations and temporal gene expression data. More specifically, Chen teaches the following aspects of the instantly claimed invention:

- Providing time series mRNA and protein concentration data [p.32], as in instant claim 1.
- Creating a non-singular diagonal matrices and generating a set of linear differential equations [p.33, lines 1-13], as in instant claims 1 and 3.
- Solutions to the linear differential equations [p.33, lines 14-19], as in instant claim 1.

CONCLUSION

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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